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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/382,837	08/25/1999	GARY E. BORODIC	BORO-101	5738

27171 7590 10/13/2005

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/382,837	BORODIC, GARY E.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 5-8, 10-12, 17-19, 21-25, and newly added Claims 42-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-8, 10-12, 17-19, 21-25, and 42-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments and remarks, filed 7/25/05, are acknowledged. In view of Applicant's amendments the previous rejection under 102(b) as being clearly anticipated by U.S. Patent No. 5,437,291 has been withdrawn.

2. Claims 1, 5-8, 10-12, 17-19, 21-25, and newly added Claims 42-57, are being acted upon.

3. The declaration stands objected to because it claims priority to Provisional Application No. 60/097,864. Applicant presumably intends to claim priority to Provisional Application No. 60/097,846 as indicated in the first line of the specification. A new declaration is required.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 17-19, 21-23 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record, specifically, the recitation of a method for treating "neurogenic inflammation". This is a new matter rejection.

Applicant's arguments, filed 7/25/05, have been fully considered but they are not persuasive. Applicant argues that the claims have been copied from the '768 patent (of record) and are subject to a request for interference.

Applicant is advised that, as set forth previously, the instant specification cannot support these claims.

6. Claims 1, 5-8, 24, 25, 42, 43, and 46-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of reducing allergy induced conjunctivitis in a mouse comprising administering a botulinum toxin,
does not reasonably provide enablement for:
A) a method of reducing inflammation without causing muscle weakness,
for the reasons of record as set forth previously.

Applicant's arguments, filed 7/25/05, have been fully considered but they are not persuasive. Applicant reiterates the assertions in the Background section of the specification and asserts, "Because the instant specification-throughout the disclosure-teaches dosing levels that reduce inflammation without producing sufficient muscle weakness and specifically doses from 1/3 to several orders of magnitude less than those associated with treatment of regional movement disorders in the corresponding muscle, the instant specification enables a skilled artisan to practice that claimed invention without undue experimentation."

As set forth previously, MPEP 2164.03 states that most physiological activity is considered to involve unpredictable factors, thus, more than a single enabled species may be required. In the instant case, *no* enabled species of the claimed method are disclosed. As set forth previously, the specification simply does not disclose that muscle weakness was ever measured. Reduced inflammation was noted only as a side effect of treatment for other disorders. Accordingly, claims drawn to reducing inflammation without causing muscle weakness, assertedly due to a new (and previously unknown) "bioeffect", must be considered to be inherently unpredictable and requiring of some sort of enablement in addition to mere assertion.

A review of the "examples" discloses: a case study of a woman treated for involuntary facial movements in which vasodilation, erythema and edema were blocked; a case study in which regional facial flushing was blocked as a result of treatment for glabelar lines; a conjunctivitis experiment in which erythema, edema, and scratching were reduced; four blepharoconjunctivitis patients in which irritation, itching, erythema and general discomfort were improved; twenty blepharospasm patients in which photophobia was mitigated; and four torticollis patients in which red patches were reduced. For *none* of these patients was it disclosed that the doses of Botox™ employed were sufficient to reduce inflammation but below that necessary to cause substantial muscle weakness. Indeed, in most of these cases it appears that Botox™ was employed in a method *intended* to cause muscle weakness and an anti-inflammatory side effect was observed. Regarding the rheumatoid arthritis and internal inflammation "examples", the specification merely asserts that the claimed method can be used to treat these conditions.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for

> patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

8. Claims 17-19 and 21-23 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,063,768 for the reasons of record as set forth previously.

Applicant has requested that an interference be declared between the instant claims and the claims of the '768 patent.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 10-12, 17-19 and 21-23, stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,063,768 (filed 9/04/97)) in view of The Merck Manual (1992) for the reasons of record as set forth previously.

Applicant has requested that an interference be declared between the instant claims and the claims of the '768 patent.

11. Claim 19 stands rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A method comprising blocking nerve and mast cell release of preformed mediators that produce permeability (Claim 19).

Applicant argues that support for the claim can be found at page 4, lines 16-18 of the specification.

Page 4, lines 16-18 of the specification discloses, "neuromuscular transmissions has also been shown to occasionally be helpful for the treatment of regional pain syndromes such as myofascial pain syndromes, headaches, and migraine headaches which can not easily be explained by the traditional chemodenervation model that has been evoked for the efficacy in regional movement diseases", which does not support the claim.

12. The following are new grounds for rejection necessitated by Applicant's amendment.

13. Claims 1, 5-8, 10-12, 17-19, 21-25, and newly added Claims 42-57, are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) A method of reducing inflammation, comprising the step of administering a therapeutically effective dose of a botulinum toxin to an affected area of a subject suffering from inflammation, wherein the botulinum toxin reduces at least one symptom of inflammation and wherein said therapeutically effective dose is sufficient to reduce said at least one symptom of inflammation but less than a dose necessary to produce substantial muscle weakness within the affected area (Claim 1).

B) A method of treating allergic blepharoconjunctivitis comprising the step of administering a therapeutically effective dose of a botulinum toxin in a periocular area of a subject suffering from blepharoconjunctivitis, thereby reducing inflammation (Claim 10).

C) A method of treating classic type I hypersensitivity comprising the step of administrating a botulinum toxin to an

affected area of a subject suffering from classic type I hypersensitivity, thereby reducing inflammation (Claim 11).

D) The method of Claim 11 whereby the hypersensitivity is hay fever, rhinitis, allergic rhinitis, allergic forms of eczema, urticaria, rheumatoid arthritis, inflammatory bowel disease, or asthma (Claim 12).

E) A method for treating inflammation, comprising the step of administering a botulinum toxin to an affected area in a therapeutically effective dose sufficient to reduce a rapid-phase response under neural regulation thereby reducing at least one symptom of inflammation, and wherein said therapeutically effective dose is sufficient to reduce the at least one symptom of inflammation but less than a dose necessary to produce substantial muscle weakness within said affected area (Claim 24).

F) The limitations of new Claims 42-57 as further limiting of Claims 1, 10, 11, and 24.

Applicant indicates that support for: A) can be found at pages 3, 4, 8, and 20; B) can be found at page 15; C) can be found at pages 11 and 12, and original Claim 12; D) can be found at page 12; E) can be found at pages 3, 4, 7, and 8; new Claims 42 and 43 at pages 9, 15, and 20; new Claims 46-48 at pages 4, 6, and 7; new Claim 49 can be found at page 12; new Claim 50 can be found at page 16; new Claims 52-53 can be found at page 3 and 4, and original Claim 2; and new Claims 54-57 at page 20 of the specification.

A review of the specification and original claims reveals that essentially no support can be found in the various cites for the limitations of the new and amended claims. First note that the cites in the Background section (pages 2-4) do not support the claimed method because neither the claimed method of the independent claims, nor any of the limitations of the dependent claims as they apply to the invention, are disclosed in the Background; if they were it would not be "background" but rather a description of the invention. Returning to the invention of Claim 1, page 8 of the specification discloses no actual method, but merely a vague teaching that, "In one embodiment, the effective dosage for allergy provoked inflammation reduction is an order of magnitude less than dosages associated with treatment of regional movement diseases,

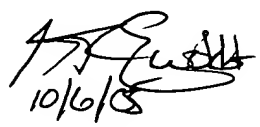
since the agent works to reduce inflammation by reducing histamine and other preformed mediator releases associated with mast cell degranulation. The effects recognized herein give new utility to chemodenervating agents." At page 20 the specification discloses only the partial results of a botulinum toxin-treated spasmodic torticollis patient and not the generic method of the claim. Similarly, the other cites do not support the newly claimed method.

14. No claim is allowed.

15. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

17. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).
Additionally, the Technology Center receptionist can be reached at (571) 272-1600.



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